Human Health and the Environment in Eastern and Central Europe

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More than 40 environmental health scientists, from 15 countries of Eastern, Central, and Western Europe and the United States, gathered from 12–15 April 1993 at Charles University in Prague, the Czech Republic, to participate in the conference, "Human Health and the Environment in Eastern and Central Europe." This conference, convened by the Conte Institute for Environmental Health, represented a unique nongovernmental effort by international scientists to develop a regional approach to research on the health effects of environmental contamination in the region.

To date, considerable money has been expended on isolated projects, with little over-all coordination of these efforts, despite the fact that the same environmental concerns are often shared by multiple countries. In addition, limited funding has been directed to the much needed improvements in equipment in Central and Eastern European laboratories and to training and educating scientific professionals.

The goals of the Prague conference were twofold: first, to develop a regional agenda for coordinated environmental health research, and second, to create a sustainable, cooperative scientific network to implement this agenda and provide the results to guide remediation efforts.

The conference opened with brief national reports, which assessed the status of environmental health and environmental health activities in each country, with priorities for future research and international cooperation. The remainder of the conference was devoted to presentation and discussion of a number of the key research and organizational issues to be considered in developing a comprehensive plan of action. Ultimately, a proposal for joint action was developed and unanimously endorsed by the participants (see below).

As the national reports were presented, there was a growing sense of the commonality of environmental health concerns among the different countries. In general, economic and industrial development since World War II has been achieved at the expense of the natural resources of the region, with dire consequences for human health. Inhabitants throughout the region have a diminished life expectancy when compared to neighboring Western Europe, ranging from 5 to 9 years lower. In addition, the numbers of congenital malformations and the incidence of cancer, cardiovascular, respiratory, and allergic diseases is alarming.

In Russia, the cancer rate has doubled in the last 20 years (to 1.6 million per year), whereas the rate of cancers in Western Europe has declined. Thousands of tons of waste are released into the air, water, and soil in Russia each year as a result of industrial accidents. Eighty-five percent of the urban population lives in territories where pollution exceeds permissible levels, and about 50% of the general population uses drinking water that does not meet hygienic requirements.

Air pollution affects approximately 17 million people in Ukraine; children living near metallurgy plants suffer from respiratory diseases twice as frequently as those residing in relatively nonindustrialized cities. A 1989 study in Ukraine found that 35% of adults and 12% of children were suffering from chronic diseases. In addition, victims of radiation exposure from the Chernobyl accident have numerous health effects, including effects on their immune system, hormonal status, cardiovascular function, and cellular regulatory systems, as well as increases in cancers and endocrine, respiratory, and neurological diseases. The rate of thyroid malignancies in children has tripled from 1989 to 1991, no doubt related to the fact that more than 60,000 children were exposed to excessive levels of internal radiation during this disaster.

Reports from Hungary, the Czech Republic, Poland, Bulgaria, Lithuania, Azerbaijan, and Germany each echoed the concerns that large segments of their populations are living in "excessively polluted" areas, enduring significant effects on human health, and that the direct linkages between exposure and effect which are needed to force legislative action and help target remediation efforts are lacking.

Poorly regulated, over-consumption of inefficient energy sources is often a major source of pollution in the region. The burning of brown coal and the use of leaded gasoline have generated unacceptable levels of lead, arsenic, oxides of nitrogen and sulfur, and dust in the environment. Contamination with cadmium, beryllium, and petroleum products is also common from the metallurgy, steel, and petrochemical industries. In agriculture, there has been widespread, indiscriminate overuse of pesticides, herbicides, and fertilizers, poisoning the soil and water with nitrates and other mutagenic substances. There are also concerns about the health effects of radionuclides, particularly of cesium^{137} released as a result of nuclear accidents, and of radon from uranium mines. While the highest levels of morbidity are associated with hot spots of pollution, the general population is also exposed to hazardous chemicals through movement of air pollution and the insidious contamination of food and water sources.

Each of the national reports stressed the need for a comprehensive, systematic approach to assessing the human health risks from environmental contamination. The recent changes in government have brought a new appreciation of the need for improved environmental health and a greater willingness to face the challenges involved in meeting that need. However, environmental health research in the region is moving much too slowly. Although, on the surface, monitoring programs appear extensive, many of them have been largely ineffective, often marked by fragmentation of responsibility among several institutions with little or no integration, no standardization and no comprehensive analytical evaluation of data, and there have been no unified standards for collection of data to allow for international comparisons. Many epidemiological studies have been limited to descriptive analyses, with insufficient attention paid to confounding factors such as genetics and lifestyle. In addition, the lack of coordination has led to a duplication of efforts in a number of cases. Opportunities for collaboration readily emerged during the conference, based on shared contaminated natural resources, equivalent exposures in geographically separate populations, and parallel but independent efforts in research development.

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This conference was organized by the Conte Institute for Environmental Health and sponsored by the March of Dimes Birth Defects Foundation (grant no. 4-FY92-1312), NIEHS (contract no. N01-ES-75185), and the Egbar Foundation.

As part of the development of a comprehensive program of research for the region, several ongoing individual research projects were presented, as were some of the experimental and organizational considerations for future research and collaboration. These special topics covered the gamut from *in vitro* genotoxic testing strategies, the application of new techniques for detecting genetic mutations and epidemiologic study considerations, to potential opportunities for funding and requirements for computer networking.

In Hungary, cytogenetic monitoring of peripheral blood lymphocytes has been used to determine whether high rates of cytogenetic changes indicate an increased risk for disease. Although children are usually more sensitive to environmental agents than adults, children actually have 40–50% lower chromosomal aberration frequencies. Among adult populations in Hungary, there is a higher rate of aberrations in rural areas than in Budapest (1.06% versus 0.88%).

A system of reproductive epidemiological studies currently in use in Hungary includes a rigorous registry network for recording congenital malformations (CMs), with compulsory reporting and with mechanisms for confirming the completeness of ascertainment and the accuracy of diagnoses. Mapping these data allows for identification of spatial clusters of CMs, based on comparison of observed and expected frequencies. A higher-than-expected frequency of CMs (aneuploidies, clefts, etc.) was linked to fish consumption in a small village after a program of chemical treatment of fish with a fungicide was instituted by the local government.

Representatives from both Russia and Lithuania described recent efforts by their governments, including the development of elaborate computer programs, to establish reliable, comprehensive registries that can be used to map the distributions of various diseases and CMs. Parallel efforts such as these underscored the need for future collaborations: not only could each nation benefit from the others in the development of useful programs, but the usefulness of any program would be greatly expanded by its universality.

The Teplice Program is a collaboration between the Czech Republic and the United States on the study of the health effects of pollution in the Northern Bohemian region of the Czech Republic. Air-quality monitoring data and biomarkers of exposure and effects in Teplice are compared with those in the less-polluted region of Prachatice. A 1991–1992 pilot study of 14–15 year olds found an increase in the prevalence of respiratory diseases and a decrease in motor coordination (finger tapping) and short-term memory (visual digit span). Human exposure was evaluated based on personal exposure monitoring and on tests for multiple biomarkers in urine and blood. The use of these types of widely accepted, standardized tests allows for global application of the results of this research.

The significance of ecological damage (ecotoxicology) as a predictor of human health effects was highlighted. Data on farm animals have revealed increased numbers of chromosomal aberrations in cows living in the industrial region of Teplice as compared to cows living in the much less polluted Prachatice. Similar differences were observed when cows and horses living in other industrial and nonindustrial regions were compared. There were also significant seasonal differences in the number of chromosomal aberrations in cows living near a large chemical plant. These studies may provide a parallel picture of what is happening to humans and may also be used to prevent food chain contamination.

The entire region of Eastern and Central Europe has a diminished life expectancy when compared to neighboring Western Europe, ranging from five to nine years lower.

Long-term, ongoing studies being done at the Urals Research Center for Radiation Medicine are assessing the human health effects of radiation exposure resulting from incidents that occurred at radio-chemical plants designed for the production of military plutonium. 1) During 1949–1952, 3 million Ci were released into the Techa River, 2) in 1957 a storage tank exploded elsewhere, releasing 20 million Ci, and 3) in 1967, 600 Ci of airborne radioactivity was detected as a result of the drying up of an open water reservoir that had been used for dumping radioactive waste. As a result of these incidents, the residents of the villages in the upper and middle reaches of the Techa received doses of 0.1–0.35 Gy, with some receiving >1 Gy, to the bone marrow. Early radiation effects were manifested as chronic radiation sickness (935 cases), and a multitude of hematologic and immunologic disorders was documented.

Long-term effects were observed only in the residents of the upper and middle reaches of the Techa. An increased incidence of cancer (especially leukemia) and an increase in general mortality have been noted in this population. In addition, risk coefficients, calculated on the basis of data on cancer mortality, have revealed a difference in risk for certain cancers between different ethnic groups. A database which was initiated in 1968 and is currently being updated contains information on over 60,000 exposed people, their offspring, and a comparison group. In contrast to studies of the atomic bomb survivors in Japan, the work at the Urals Research Center may provide a unique source of information about the long-term effects of chronic exposure to low to medium doses of radiation.

Recommendations for future research in the region focused on the need for population-based epidemiology to sort out confounding variables, such as genetics and lifestyle, and on molecular studies with attention to genetic damage, cytogenetic abnormalities, and other preclinical indicators of exposure and effect such as defects in DNA repair and polymorphisms of enzymes involved in the metabolism of xenobiotics (e.g., P450 and acetylator enzymes). The expansion of registries and sharing of databases across national boundaries will facilitate future efforts. In addition, a successful regional program will require mechanisms for quality assurance and quality control and for general agreement within the region and with Western Europe and the United States on standards for chemical safety, environmental health monitoring and record keeping, and research methods.

Four general areas for monitoring genetic mutations were suggested: tumors of childhood (e.g., retinoblastoma, Wilm's tumor), diseases involving trinucleotide repeats (e.g., Huntington's), VTR mutations (e.g., minisatellite repeats in cancer), and clotting factor deficiencies. Family studies of genetic mutations will help to identify somatic mutations which enter the germline, and international databases of gene mutations may reveal which mutations are environmentally induced.

The EPA/International Agency for Research on Cancer program uses short-term *in vivo* and *in vitro* testing, in increasingly sophisticated systems, to generate an "activity profile" (bar graph) for each compound based on lowest effective and highest ineffective doses. Computer integration of these data from different compounds

provides useful information about the genetic toxicity and related effects of complex mixtures. The IARC database, which contains information on many chemicals, requires minimal computer capabilities and is publicly available.

A general overview of current funding opportunities for environmental health research in Central and Eastern Europe, through the United States and within the region, revealed that although there has been some increase in support in recent years, the amount of funding for environmental health research in Central and Eastern Europe falls far short of the need, and no major increases are projected. As an example, the Hungarian government is currently allowing $42,000 of support for 3 years for 12 projects. Only 2% of the total U.S. National Institutes of Health budget for biomedical research in the region ($6 million) is allocated for environmental health research, and this funding often takes 1–1.5 years to obtain. Much work and funding is needed to bring the laboratories in the region up to speed. Many of the Central and Eastern European investigators expressed a need for training in how to apply for funding from the United States and suggested that courses on applying for funding and on developing common standards for data collection would be helpful.

Representatives of WHO, the Centre National de la Recherche Scientifique (CNRS), and the Commission of European Communities (EC) outlined their programs and expressed their support for this effort. EC funding (but not participation) is limited at present to laboratories and institutes in the EC. There is a new program of research cooperation with Central and Eastern European countries whereby EC funds could be made available to help laboratories in those countries participate in existing EC projects. To obtain EC research funding, the legal base of operations should be in an EC member state.

The final hours of the conference were devoted to establishing a preliminary proposal for action on environmental health research in the region. A list of priorities for research, which encompassed a wide range of priorities suggested during the conference, was presented. Six areas for action were unanimously supported by the group:

- Research into the effects of toxic metals (e.g. lead, cadmium, arsenic, and beryllium);
- Research on the populations of the region on cancer, birth defects, and other diseases, with emphasis on data sharing across national boundaries; on quality control; and on use of biomarkers of reproductive and other effects;
- Studies on the molecular, biochemical, and chromosomal bases for varying susceptibilities to environmentally induced diseases;
- Coordination of research on radiation effects, especially on radiation exposures resulting from nuclear power and weapons plants;
- Research on approaches to bioremediation; and
- Education and training of professionals and nonprofessionals in environmental health issues, on an international basis.

A proposed mission statement for the future organization of this international scientific effort and a steering committee for establishment of the International Scientific Committee on Environmental Health were presented. (The committee was officially incorporated as the Comite International de Scientifiques pour la Sante et l'Environment, in Paris, November 1993.) These proposals were unanimously endorsed, laying the groundwork for establishment of a unified international scientific network for cooperation on environmental health research in Central and Eastern Europe.